Claims

1. A method for making composite active particles for use in a pharmaceutical composition for pulmonary inhalation, the method comprising jet milling active particles in the presence of particles of additive material and, optionally, air or a compressible gas or fluid.

2. A method as claimed in claim 1, wherein the additive material comprises an amino acid, a metal stearate or a phospholipid.

3. A method as claimed in claim 2, wherein the additive material comprises one or more of leucine, isoleucine, lysine, valine, methionine, phenylalanine.

4. A method as claimed in claim 3, wherein the additive material comprises leucine and preferably L-leucine.

5. A method as claimed in claim 2, wherein the additive material comprises magnesium stearate.

6. A method as claimed in claim 2, wherein the additive material comprises lecithin.

7. A method as claimed in any one of the preceding claims, wherein the jet milling is carried out at an inlet pressure of between 0.1 and 3 bar.

8. A method as claimed in any one of claims 1-6, wherein the jet milling is carried out at an inlet pressure of between 3 and 12 bar.

9. A method as claimed in any one of the preceding claims, wherein at least 90% by volume of the active particles are less than 20μm in diameter prior to jet milling.

10. A method as claimed in any one of the preceding claims, wherein at least 90% by volume of the additive particles are less than 20μm in diameter prior to jet milling.

11. A method as claimed in any one of the preceding claims, wherein jet milling is carried out at temperatures below room temperature.

12. A method as claimed in claim 11, wherein jet milling is carried out at a temperature below 10°C and preferably below 0°C.

13. A method as claimed in any one of the preceding claims, wherein carrier particles are also jet milled with the active particles and the particles of additive material.

14. A method as claimed in claim 13, wherein the carrier particles have a particle size of at least 20μm.

15. A method as claimed in claim 13, wherein the carrier particles have a particle size of less than 30μm, preferably less than 20μm and more preferably less than 10μm.

16. Composite active particles for use in a pharmaceutical composition made using a method as claimed in any one of the preceding claims.

17. Composite active particles as claimed in claim 16, for pulmonary inhalation.

18. Composite active particles as claimed in either of claims 16 and 17, wherein the additive material forms a coating on the surface of the additive particles.

19. Composite active particles as claimed in claim 18, wherein the coating is a discontinuous coating.

20. Composite active particles as claimed in either of claims 18 and 19, wherein the coating of additive material is not more than 1μm in thickness.

21. Composite active particles as claimed in any one of claims 16-20, having an MMAD of not more than 10μm.

22. Composite active particles as claimed in claim 21, having an MMAD of not more than 5μm, not more than 3μm, not more than 2μm, or not more than 1μm.

23. Composite active particles as claimed in any one of claims 16-22, wherein at least 90% by weight of the composite active particles have a diameter of not more than 10μm.

24. Composite active particles as claimed in claim 23, wherein at least 90% by weight of the particles have a diameter of not more than 5μm, not more than 3μm, or not more than 1μm.

25. A pharmaceutical composition comprising composite active particles as claimed in any one of claims 16-24.

26. A composition as claimed in claim 25, wherein the composition is for pulmonary inhalation.

27. A composition as claimed in either of claims 25 and 26, wherein the composition is a dry powder composition.

28. A composition as claimed in claim 27, wherein the composition further comprises carrier particles.

29. A composition as claimed in any one of claims 25-28, wherein the composition has a FPF(ED) of at least 70%.

30. A composition as claimed in claim 29, wherein the FPF(ED) is at least 80%, at least 85%, or at least 90%.

31. A composition as claimed in any one of claims 25-28, wherein the composition has a FPF(MD) of at least 60%.

32. A composition as claimed in claim 29, wherein the FPF(MD) is at least 70%, at least 80%, or at least 85%.

33. A dry powder inhaler containing a composition as claimed in any one of claims 25-32.

34. Use of an additive material as a milling aid in the jet milling of an active material.